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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,146	01/17/2002	Bernhard Hauer	50915	6323

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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/031,146	HAUER ET AL.	
	Examiner	Art Unit	
	YONG D. PAK	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12-14 and 16-24* is/are pending in the application.

4a) Of the above claim(s) *1-8,13,14,16 and 19-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,10,12,17 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a 371 of PCT/EP00/07253.

The amendment filed on June 29, 2009, amending claims 9-10 and 12, has been entered.

Claims 1-10, 12-14 and 16-24 are pending. Claims 1-8, 13-14, 16 and 19-24 are withdrawn. Claims 9-10, 12 and 17-18 are under consideration.

Response to Arguments

Applicant's amendment and arguments filed on June 29, 2009, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

In view of applicant's argument, the rejections of claim 9 and claims 10, 12 and 17-18 depending therefrom under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention have been **withdrawn**.

Claims 17-18 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 17-18 recite the phrase "wherein, as exogenous substrate". The metes and bounds of this phrase are not clear to the Examiner. Literally, the phrase means a "like" or "similar" to an "exogenous substrate". Therefore, it is not clear to the Examiner either from the specification or form the claims as to what applicants mean by the above phrase. It appear that applicants have meant to recite "wherein the exogenous substrate is selected from..". Examiner requests clarification of the above phrase.

Applicants did not provide any arguments. Therefore, the rejection is **maintained**.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-10, 12 and 17-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 9-10, 12 and 17-18 are drawn to a method of oxidizing N- or S-heterocyclic mono- or polynuclear aromatic compounds using cytochrome P450

monooxygenase derived from SEQ ID NO:2 and comprising at least one mutation in at least one of the regions recited in claim 9. The claim recites the language "at least functional mutation in at least one of the amino acid sequence regions", it is interpreted as any single or any number of mutations in at least one of the recited regions. Further, the claims are not limited to a variant of SEQ ID NO:2 consisting of mutations at the recited regions, but to any variant or mutant of SEQ ID NO:2 comprising of mutations at the recited regions and any other mutations at other regions. The limitation of comprising "at least functional mutation in at least one of the amino acid sequence regions" provides no description on the structure of other parts of the enzyme. Thus the claims encompass a method of oxidizing any or all N- or S-0 heterocyclic mono- or polynuclear aromatic compounds using any variants, mutants and recombinants of SEQ ID NO:2 comprising any number of mutations at the recited regions and in other regions. Therefore, the claims are drawn to a method of oxidizing a genus of N- or S-0 heterocyclic mono- or polynuclear aromatic compounds having any structure using any or all cytochrome P450 monooxygenase derived from SEQ ID NO:2, including any or all recombinants, mutants and variants, including those that comprise mutations at the recited regions. The specification only describes one representative species, a method for oxidizing indoles with a modified cytochrome P450 monooxygenase of SEQ ID NO:2 having mutations at residue Phe87Val, Phe87Val and Leu 188Gin, or Phe87Val, Leu188Gln and Ala74Gly expressed in a host cell comprising a polynucleotide encoding said modified monooxygenases. One species is not enough and does not constitute a representative number of species to describe the whole genus and there is no evidence

on the record of the relationship between the structure of indoles and the structure of any or all N- or S-0 heterocyclic mono- or polynuclear aromatic compounds. Similarly, there is no evidence on the record of the relationship between the structure of SEQ ID NO:2 and the structure of any cytochrome P450 monooxygenase derived from SEQ ID NO:2, including any or all recombinants, variants and mutants. Therefore, the specification fails to describe a representative species of the genus comprising any or all variants, mutants or recombinants of SEQ ID NO:2 used in the method of oxidizing a genus of any or all N- or S-0 heterocyclic mono- or polynuclear aromatic compounds.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan Would recognize that applicants were in possession of the inventions of claims 9-10, 12 and 17-18.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office Action, applicants have traversed the above rejection.

It appears that applicants have grouped arguments against the written description requirement and the enablement requirement together. applicant's arguments addressing undue experimentation is rebutted below in the enablement rejection.

Applicants argue that even one example may satisfy the written description. As discussed above, while MPEP 2163 acknowledges that in certain situations "one species adequately supports a genus," it also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus." In the instant application, the claims encompass a method of oxidizing any or all N-or S-heterocyclic mono or polynuclear aromatic compounds and any or all secondary product(s) thereof or the oxidation of the substrates recited in claim 18 using any or all mutant cytochrome P450 monooxygenase having unknown structure, except for having Phe87Val, Phe87Val and Leu 188Gln, or Phe87Val, Leu188Gln and Ala74Gly substitution(s). Thus, in view of the widely variant species encompassed by the genus, said one species is not enough and does not constitute a representative number of species to describe a method of oxidizing a genus comprising any or all N-or S-heterocyclic mono or polynuclear aromatic compounds and any or all secondary product(s) thereof or the oxidation of the substrates recited in claim 18 using a genus comprising any or all mutant cytochrome P450 monooxygenase having unknown structure, except for having Phe87Val, Phe87Val and Leu 188Gln, or Phe87Val, Leu188Gln and Ala74Gly substitution(s).

As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical

and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only a few species within the genus. In the instant case the claimed genera of the claims includes species which are widely variant in structure. The claims are drawn to structurally diverse species as it encompasses a method of oxidizing heterocyclic mono or polynuclear aromatic compounds and any or all secondary product(s) thereof or the oxidation of the substrates recited in claim 18 using a genus comprising any or all mutant cytochrome P450 monooxygenase having unknown structure, except for having Phe87Val, Phe87Val and Leu 188Gln, or Phe87Val, Leu188Gln and Ala74Gly substitution(s). As such, the description of solely functional features present in all members of the genus is insufficient to be representative of the attributes and features of the entire genus.

Hence the rejection is maintained.

Claims 9-10, 12 and 17-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of microbiological oxidation of N-or S-heterocyclic mono or polynuclear aromatic compounds by using a modified cytochrome P450 monooxygenase of SEQ ID NO:2 having a Phe87Val, Phe87Val and Leu 188Gln, or Phe87Val, Leu188Gln and Ala74Gly substitution with indole as a substrate, does not reasonably provide enablement for A) a method for oxidation of any or all N-or S-heterocyclic mono or polynuclear aromatic compounds and B) a method for oxidation of any or all N-or S-heterocyclic mono or polynuclear aromatic compounds with any modified P450 monooxygenase having one or more functional mutation in one of the regions corresponding to 172-224, 39-43, 48-52, 67-70, 330-335, 352-356, 73-82 and 86-88 of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 9-10, 12 and 17 are drawn to a method for the oxidation of any or all N-or S-heterocyclic mono or polynuclear aromatic compounds with any modified cytochrome

P450 monooxygenase derived from *Bacillus megaterium* having one more functional mutation in one or more of the regions corresponding to residues 172-224, 39-43, 48-52, 67-70, 330-335, 352-356, 73-82 and 86-88 of SEQ ID NO:2, which amounts substituting 1 to 91 amino acids, or a modified cytochrome P450 monooxygenase with SEQ ID NO:2 having a Phe87Val, Phe87Val and Leu 188Gln, or Phe87Val, Leu188Gln and Ala74Gly substitution. Claim 18 is drawn to a method for the oxidation of an indole with a modified cytochrome P450 monooxygenase derived from *Bacillus megaterium* having one more functional mutation in one or more of the regions corresponding to residues 172-224, 39-43, 48-52, 67-70, 330-335, 352-356, 73-82 and 86-88 of SEQ ID NO:2. Therefore, the claims encompass a method for the oxidation of any or all N-or S-heterocyclic mono or polynuclear aromatic compounds using a modified cytochrome P450 monooxygenase derived from *Bacillus megaterium* having a large number of amino acid substitution, resulting in an enzyme that oxidizes heterocyclic or mono or polynuclear aromatic compounds.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of N-or S-heterocyclic mono or polynuclear aromatic compounds and P450 monooxygenase variants and mutants, broadly encompassed by the method of the claims. The claims encompass compounds with widely varying structure and properties. However, in this case the disclosure is limited to a method for oxidizing indoles with a modified cytochrome P450 monooxygenase of SEQ ID NO:2 having mutations at residue Phe87Val, Phe87Val and Leu 188Gln, or Phe87Val, Leu188Gln and Ala74Gly expressed in a host cell comprising

a polynucleotide encoding said modified monooxygenases. It would require undue experimentation of the skilled artisan to oxidize any N-or S-heterocyclic mono or polynuclear aromatic compounds.

Further, since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to a method for oxidizing an indole with a modified cytochrome P450 monooxygenase of SEQ ID NO:2 having mutations at residue Phe87Val, Phe87Val and Leu 188Gln, or Phe87Val, Leu188Gln and Ala74Gly expressed in a host cell comprising a polynucleotide encoding said modified monooxygenases. It would require undue experimentation of the skilled artisan to make and use the claimed variants and mutants of any P450 monooxygenases. In view of the great breadth of the claim, amount of experimentation required to make the claimed polynucleotides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple

modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass a method for the oxidation of any or all any N-or S-heterocyclic mono or polynuclear aromatic compounds using any or all mutants and variants of any P450 monooxygenase, because the specification does not establish: (A) amino acids of any P450 monooxygenase which may be modified without affecting P450 monooxygenase activity and having an altered substrate specificity, i.e. oxidizing N-or S-heterocyclic mono or polynuclear aromatic compounds; (B) the general tolerance of P450 monooxygenase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function; (D) any or all any N-or S-heterocyclic mono or polynuclear aromatic compounds which are oxidized by a modified P450 monooxygenases; (E) a rational and predictable scheme for selecting any N-or S-heterocyclic mono or polynuclear aromatic compounds with an expectation of obtaining oxidized any N-or S-heterocyclic mono or polynuclear aromatic compounds by incubating said substrates with a modified P450 monooxygenase; and (F) the

specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a method for the production of any or all any N-or S-heterocyclic mono or polynuclear aromatic compounds using any or all variants and mutants of any P450 monooxygenase. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of mutants and variants of any P450 monooxygenase having the desired biological characteristics recited in the claim is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that the claims meet the enablement requirement because one of ordinary skill in the art would not require undue experimentation to create the instant invention because the art at the time of filing would allow said creation, applicants are entitled to the whole range of embodiments made available without undue experimentation, and applicants created functionally mutated P450 BM03 proteins which have the ability to produce blue indigo-containing pigment. Examiner respectfully disagrees. The claims are not limited to a method of oxidizing specific substrates or

indiole using specific mutants of SEQ ID NO:2 but a method of oxidizing any or all N-or S-heterocyclic mono or polynuclear aromatic compounds and any or all secondary product(s) thereof or the oxidation of the substrates recited in claim 18 using any or all mutant cytochrome P450 monooxygenase having at least one functional mutation in at least one of the amino acid sequence regions 172-224, 39-43, 48-52, 67-70, 330-335, 352-356, 73-82 and 86-88 of SEQ ID NO:2 or Phe87Val, Phe87Val and Leu 188Gln, or Phe87Val, Leu188Gln and Ala74Gly substitution(s). The limitation of "having" at least one functional mutation in at least one of the amino acid sequence regions 172-224, 39-43, 48-52, 67-70, 330-335, 352-356, 73-82 and 86-88 of SEQ ID NO:2 or Phe87Val, Phe87Val and Leu 188Gln, or Phe87Val, Leu188Gln and Ala74Gly substitution(s) provides no description on the structure of other parts of the mutant cytochrome P450 monooxygenase because the claimed variant is not limited to only those substitutions at positions 172-224, 39-43, 48-52, 67-70, 330-335, 352-356, 73-82 and 86-88 of SEQ ID NO:2. Therefore, while the variant comprises the recited substitutions, the same variant comprises any amino acids in any other positions. Therefore, the claims encompass a method of using polypeptides molecules having unknown structure except having Phe87Val, Phe87Val and Leu 188Gln, or Phe87Val, Leu188Gln and Ala74Gly substitution(s). As discussed above, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a specific knowledge of and guidance with regard to which specific amino acids in the protein's sequence, can be modified such that the modified polypeptide continues to have said claimed activity. It is this specific guidance that applicants do not provide. While the art

may teach in general the structure of the cytochrome P450 monooxygenase of SEQ ID NO:2, conserved amino acid sequences, x-ray crystal structure and etc, such teachings will not reduce the burden of undue experimentation on those of ordinary skill in the art.

Hence the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 9-10, 12 and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Wong et al.

Claims 9-10, 12 and 17 are drawn to a method of oxidizing N-or S-heterocyclic mono or polynuclear aromatic compounds with a modified cytochrome P450 monooxygenase derived from *Bacillus megaterium* having a mutation corresponding to residue 87 of SEQ ID NO:2.

Wong et al. (GB 2 294 692 - form PTO-1449) discloses a method of oxidizing N-heterocyclic polynuclear aromatic compound with a modified cytochrome P450 monooxygenase having a mutation corresponding to residue 87 of SEQ ID NO:2. (abstract and pages 4 and 14). The method of Wong et al. uses a modified cytochrome P450 monooxygenase that is "derived from *Bacillus megaterium*". Therefore, the reference of Wong et al. anticipates claims 9-10, 12 and 17.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that Wong et al. does not anticipate the instant claims because (1) the second paragraph on page 4 of GB 2 294 692 makes clear the range of substrates as polycyclic aromatic hydrocarbons and (2) heterocyclic compounds serve as protection groups for the oxidation of said range of polycyclic aromatic hydrocarbons. Examiner respectfully disagrees. (1) the second full paragraph of page 4 is one embodiment. Wong et al. discloses that "various classes of organic compounds are envisaged" including aromatic compounds. Therefore, the substrates of Wong et al. are not limited to only polycyclic aromatic hydrocarbons. (2) The instant claims do not recite the oxidized product, but merely a method for the oxidation of a N-heterocyclic mono or polynuclear aromatic compound. Therefore, the claims encompass a method of

oxidizing aromatic compounds comprising N-heterocyclic protecting groups. Even though claims are interpreted in light of the specification, it is improper to import claim limitations from the specification and claims must be given their broadest reasonable interpretation, see MPEP 2111 and 2111.01. Therefore, since the substrates of Wong et al. are N-heterocyclic mono or polynuclear aromatic compounds and Wong et al. teaches a method of oxidizing said compounds, the reference of Wong et al. anticipates the instant claims. Hence the rejection is maintained.

Claims 9-10, 12 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Wong et al.

Claims 9-10, 12 and 17 are drawn to a method of oxidizing N-or S-heterocyclic mono or polynuclear aromatic compounds with a modified cytochrome P450 monooxygenase derived from *Bacillus megaterium* having a mutation corresponding to residue 87 of SEQ ID NO:2.

Wong et al. (U.S. Patent No. 6,100,074 - form PTO-1449) discloses a method of oxidizing N-heterocyclic polynuclear aromatic compound with a modified cytochrome P450 monooxygenase having a mutation corresponding to residue 87 of SEQ ID NO:2. (Columns 3-6 and claims 8-11). The method of Wong et al. uses a modified cytochrome P450 monooxygenase that is "derived from *Bacillus megaterium*". Therefore, the reference of Wong et al. anticipates claims 9-10, 12 and 17.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that Wong et al. does not anticipate the instant claims because (1) Column 2, lines 38-47 makes clear the range of substrates as polycyclic aromatic hydrocarbons and (2) heterocyclic compounds serve as protection groups for the oxidation of said range of polycyclic aromatic hydrocarbons. Examiner respectfully disagrees. (1) Column 2, lines 38-47 is one embodiment. Wong et al. discloses that "various classes of organic compounds are envisaged" including aromatic compounds. Therefore, the substrates of Wong et al. are not limited to only polycyclic aromatic hydrocarbons. (2) The instant claims do not recite the oxidized product, but merely the oxidation of a N-heterocyclic mono or polynuclear aromatic compound. Therefore, the claims encompass a method of oxidizing aromatic compounds comprising N-heterocyclic protecting groups. Even though claims are interpreted in light of the specification, it is improper to import claim limitations from the specification and claims must be given their broadest reasonable interpretation, see MPEP 2111 and 2111.01. Therefore, since the substrates of Wong et al. are N-heterocyclic mono or polynuclear aromatic compounds and Wong et al. teaches a method of oxidizing said compounds, the reference of Wong et al. anticipates the instant claims. Hence the rejection is maintained.

Conclusion

None of the claims are allowable.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Yong D Pak/
Primary Examiner, Art Unit 1652